

PCT

FEILER, William S.
Morgan & Finnegan
345 Park Avenue
New York, New York 10154
ETATS-UNIS D'AMERIQUE

RECEIVED
CLOCK DEPT.

(PCT Rule 66)

MAY 28 1997

MORGAN & FINNEGAN
MORGAN & FINNEGAN

Date of mailing
(day/month/year)

23. 05. 97.

REPLY DUE

within 3 months/days
from the above date of mailing

International filing date (day/month/year)

Priority date (day/month/year)

16/08/1996

18/08/1995

International Patent Classification (IPC) or both national classification and IPC

C12N15/16

Applicant

DEPARTMENT OF HEALTH AND HUMAN SERVICES et al.

1. This written opinion is the final (first, etc.) drawn up by this International Preliminary Examining Authority.
2. This report contains indications and corresponding pages relating to the following items:

- I ☒ Basis of the opinion
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

nt
CASE 2026-4202 PC ATTN LAS

- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international appl

DUE Aug. 23, 1997

1 mo. call-up July 23, 1997

Written-Opinion BY (74)

- 3. The applicant is hereby invited to reply to this opinion.**

When? See the time limit indicated above. The applicant may, before the expiration of that time limit, request this Authority to grant an extension, see Rule 66.2(d).

How? By submitting a written reply, accompanied, where appropriate, by amendments, according to Rule 66.3. For the form and the language of the amendments, see Rules 66.8 and 66.9.

Also For an additional opportunity to submit amendments, see Rule 66.4.
For the examiner's obligation to consider amendments and/or arguments, see Rule 66.4*bis*.
For an informal communication with the examiner, see Rule 66.6.

If no reply is filed, the international preliminary examination report will be established on the basis of this opinion.

4. The final date by which the international preliminary examination report must be established according to Rule 69.2 is: 18/12/1997

Name and mailing address of the IPEA;

Authorized officer

A. H. Anderson - Fred

EL 853 256 591 US

WRITTEN OPINION

Intern. application No.
PCT/US96/13286

I. Basis of the opinion

1. This opinion has been drawn up on the basis of (Substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this opinion as "originally filed".):

☐ the international application as originally filed.

☒ the description, pages 1-72 _____, as originally filed,
pages _____, filed with the demand,
pages _____, filed with the letter of _____,

☒ the claims, Nos. 7(in part), 8-16 _____, as originally filed,
Nos. 1-6, 7(in part) _____, as amended under Article 19,
Nos. _____, filed with the demand,
Nos. _____, filed with the letter of _____,

☒ the drawings, sheets/fig 1/26-26/26 _____, as originally filed,
sheets/fig _____, filed with the demand,
sheets/fig _____, filed with the letter of _____,

2. The amendments have resulted in the cancellation of:

☐ the description, pages _____.

☐ the claims, Nos. _____.

☐ the drawings, sheets/fig _____.

3. ☐ This opinion has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

WRITTEN OPINION

Intern. application No.

PCT/US96/13286

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been and will not be examined in respect of:

☐ the entire international application,

☒ claims Nos. 3,4,7,10-13 and 8,9,14 partially_____

because:

☒ the said international application, or the said claims Nos. 3,4,7,10-13 and 8,9,14 partially_____ relate to the following subject matter which does not require an international preliminary examination (specify):

Method for treatment of the human or animal body by therapy as well as diagnostic methods (Rule 67.1 (iv) PCT), as far as they concern an in-vivo method.

☐ the description, claims or drawings (indicate particular elements below) or said claims

Nos. _____ are so unclear that no meaningful opinion could be formed (specify):

☐ the claims, or said claims Nos. _____ are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for said claims

Nos. _____.

WRITTEN OPINION

Intern. application No.
PCT/US96/13286

V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step and industrial applicability; citations and explanations supporting such statement

1. STATEMENT

Novelty (N)	Claims 1,2,5,6,15,16 and 8,9,14(all in part):yes____ Claims _____
Inventive Step (IS)	Claims 1,2,5,6,15,16 and 8,9,14 (all in part):no____ Claims _____
Industrial Applicability (IA)	Claims 1,2,5,6,15,16 and 8,9,14 (all in part): yes____ Claims _____

2. CITATIONS AND EXPLANATIONS

1. The following documents are mentioned for the first time in this written opinion; the numbering is identical to the order used in the International Search Report and will be adhered to in the rest of the procedure:

D1 to D3

2. D1 discloses in claims ~~19~~¹⁷ a peptide having a catecholamine secretion inhibitory effect comprising an amino acid sequence from Ala in the 73-position to Arg in the 54-position of SEQ ID No.1 and in claim 22 a peptide comprising an amino acid sequence from Trp in the -61 position to Arg in the -54 position of SEQ id No.1, the peptide generating an antibody recognizing the amino acid sequence of claim 19. D1 further discloses in Example 7 the isolated peptides [(-73)-(-54)] and [(-61)-(-54)] being used as an antigen and were found to be useful in the production of an antibody against pro-AM-N20.

Therefore novelty of present Seq. ID 7 according to claim 1 is lacking.

Novelty of Seq. ID 3 according to claim 1 is present since the peptide [(-61)-(-54)] has been elongated at the N-terminus by YY , novelty of Seq. ID 1 and 2 is also present, since although the sequences disclosed fall within the SEQ ID according to D1, they have not been disclosed explicitly. However it has to be added that in studying D1 at least the C-terminus of SEQ ID 3 has been several times explicitly be indicated as position 52 in claims 1 to 7 of D1.

3. As far as the requirements of inventive step are concerned it would appear that the activity mentioned in D1 and the activity mentioned in the application respond to the same physiological system describing different effects of the same system. In fact effects described in D1 showing a vasorelactant activity, catecholamine secretion inhibitory effect and Na channel inhibitory effect seem to be effective in other diseases than cardiac failure, cardiac infraction and hypertension, in diseases mentioned in the application like diabetes, renal diseases, such as severe uremia, bone diseases, skin diseases and blood diseases.

Therefore with the technical information at present in this file when compared with D1, which is considered to represent the closest prior art document, it would appear that the activities mentioned in the application could have been deduced in an obvious manner from a study of D1 in an obvious manner, the modification/selection of the sequences claimed seems to form part of routine laboratory work.

D2 refers to the 52 amino acid peptide adrenomedullin in amidated form, D3 relates to different peptides that include conformation ocnstraining groups which flank a protein-protein interaction site in different type of

hypotensive peptides. Therefore these documents represent a more general prior art.

4. For the assessment of the present Claims 3,4,7,10-13 and 8,9,14 (in part) on the question whether they are industrially applicable, no unified criteria exist in the PCT. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but will allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.
5. To meet the requirements of Rule 5.1(a)(ii) PCT, the document D1 should be identified in the description and the relevant background art disclosed therein should be briefly discussed.

INTERNATIONAL SEARCH REPORT

International Application No.
PCT/US 96/13286

A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 C12N15/16 C07K14/575 C07K7/06 C07K7/08 C07K16/26
A61K38/08 A61K38/10 A61K38/22 A61K39/395 G01N33/53
C12Q1/68

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 C07K C12N A61K G01N C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP,A,0 622 458 (SHIONOGI & CO ;KANGAWA KENJI (JP)) 2 November 1994 see page 2, line 5 - line 15 see page 2, line 29 - page 3, line 56 see page 4, line 5 - line 44 see page 8, line 11 - page 9, line 6 see page 9, line 25 - line 40 --- -/--	1,2,5,6, 15,16



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
- *&* document member of the same patent family

Date of the actual completion of the international search

20 January 1997

Date of mailing of the international search report

29. 01. 97

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+ 31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+ 31-70) 340-3016

Authorized officer

Montero Lopez, B

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 96/13286

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>EIGHTY-SIXTH ANNUAL MEETING OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH, TORONTO, ONTARIO, CANADA, MARCH 18-22, 1995. PROCEEDINGS OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH ANNUAL MEETING 36 (0). 1995. 265. ISSN: 0197-016X, XP002017893</p> <p>MARTINEZ A ET AL: "Adrenomedullin, a new hypotensive peptide, is expressed in normal lung and in pulmonary tumors." see abstract no. 1580</p> <p>---</p>	5
A	<p>WO,A,94 25482 (EVANS, HERBERT, J. ET AL.) 10 November 1994 see page 22, line 7 - line 22</p> <p>-----</p>	1,15

INTERNATIONAL SEARCH REPORT

International Application No.

PCT/US 96/13286

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP-A-0622458	02-11-94	JP-A- 7196693 AU-A- 6064894 CA-A- 2122112	01-08-95 27-10-94 27-10-94
-----	-----	-----	-----
WO-A-9425482	10-11-94	AU-A- 6770794 CA-A- 2161108	21-11-94 10-11-94
-----	-----	-----	-----

EL 853 256 591 US

09-10-1998



100825483

PATENT

Docket No. 2026-4202US3

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s) : Frank Cuttitta et al.

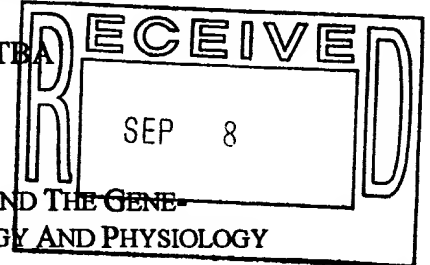
Group Art Unit: TBA

Serial No. : 09/011,922

Examiner: TBA

Filed : February 17, 1998

For : FUNCTIONAL ROLE OF ADRENOMEDULLIN (AM) AND THE GENE-RELATED PRODUCT (PAMP) IN HUMAN PATHOLOGY AND PHYSIOLOGY



Assistant Commissioner for Patents
BOX ASSIGNMENT
Washington, D.C. 20231

RECORDATION FORM COVER SHEET
PURSUANT TO 37 C.F.R. §§ 3.28 AND 3.31

Sir:

Please record the attached original documents or copy thereof.

1. Name of conveying party/parties:

Frank Cuttitta, Alfredo Martinez, Mae Jean Miller, Edward J. Unsworth,
William Hook, Thomas Walsh, Karen Gray, and Charles Macri

2. Name and address of receiving party/parties:

Name: The National Institutes of Health, as represented by the Secretary,
Department of Health and Human Services

Internal Address: Office of Technology Transfer

Street Address: 6011 Executive Boulevard, Suite 325

City Rockville State Maryland Country USA ZIP 20852

[] Additional names and addresses attached.

3. Nature of Conveyance:

☒ Assignment ☐ Merger ☐ Security Agreement
☐ Change of Name ☐ Other _____

Execution Date: August 11, 1998

09/10/1998 SSMITH

01 70-001

09000000 09011900

4060

TB 608 954 896 US

EL 853 256 591 US

MRD 9-8-98

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AM	Armenia	GB	United Kingdom	MW	Malawi
AT	Austria	GE	Georgia	MX	Mexico
AU	Australia	GN	Guinea	NE	Niger
BB	Barbados	GR	Greece	NL	Netherlands
BE	Belgium	HU	Hungary	NO	Norway
BF	Burkina Faso	IE	Ireland	NZ	New Zealand
BG	Bulgaria	IT	Italy	PL	Poland
BJ	Benin	JP	Japan	PT	Portugal
BR	Brazil	KE	Kenya	RO	Romania
BY	Belarus	KG	Kyrgyzstan	RU	Russian Federation
CA	Canada	KP	Democratic People's Republic of Korea	SD	Sudan
CF	Central African Republic	KR	Republic of Korea	SE	Sweden
CG	Congo	KZ	Kazakhstan	SG	Singapore
CH	Switzerland	LI	Liechtenstein	SI	Slovenia
CI	Côte d'Ivoire	LK	Sri Lanka	SK	Slovakia
CM	Cameroon	LR	Liberia	SN	Senegal
CN	China	LT	Lithuania	SZ	Swaziland
CS	Czechoslovakia	LU	Luxembourg	TD	Chad
CZ	Czech Republic	LV	Latvia	TG	Togo
DE	Germany	MC	Monaco	TJ	Tajikistan
DK	Denmark	MD	Republic of Moldova	TT	Trinidad and Tobago
EE	Estonia	MG	Madagascar	UA	Ukraine
ES	Spain	ML	Mali	UG	Uganda
FI	Finland	MN	Mongolia	US	United States of America
FR	France	MR	Mauritania	UZ	Uzbekistan
GA	Gabon			VN	Viet Nam

4. Application Number(s) or Patent Number(s):

[] This document is being filed together with a new application filed concurrently herewith and which was executed on _____.

[X] Patent Application No.(s) 09/011,922, filed February 17, 1998.

5. Address all future communications to:

William S. Feiler, Esq.
MORGAN & FINNEGAN, L.L.P.
345 Park Avenue
New York, New York 10154-0053

6. Total number of applications and patents involved: 1

7. Total fee (37 CFR §§3.41 and 1.21(h)):

\$40.00 per property x 1 property(ies) = \$ 40.00

[X] A check in the amount of \$ 40.00 to cover the recordation fee is enclosed.

[] Charge fee to Deposit Account No. 13-4500. Order No. _____.

8. [X] The Commissioner is hereby authorized to charge any additional fees which may be required for this recordation, or credit any overpayment to Deposit Account No. 13-4500. Order No. 2026-4202US3.

9. To the best of my knowledge and belief, the foregoing information is true and correct and any attached copy is a true copy of the original document.

Respectfully submitted,
MORGAN & FINNEGAN, L.L.P.

Dated: September 4, 1998

By: Leslie A. Serunian
Leslie A. Serunian
Registration No. 35,353

Correspondence Address:

MORGAN & FINNEGAN, L.L.P.
345 Park Avenue
New York, New York 10154-0053
(212) 758-4800
(212) 751-6849 Facsimile

Total number of pages comprising this
cover sheet 7



UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
ASSISTANT SECRETARY AND COMMISSIONER
OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

DECEMBER 29, 1998

PTAS

MORGAN & FINNEGAN, L.L.P.
WILLIAM S. FEILER, ESQ.
345 PARK AVENUE
NEW YORK, NY 10154-0053



100825483A

UNITED STATES PATENT AND TRADEMARK OFFICE
NOTICE OF RECORDATION OF ASSIGNMENT DOCUMENT

THE ENCLOSED DOCUMENT HAS BEEN RECORDED BY THE ASSIGNMENT DIVISION OF THE U.S. PATENT AND TRADEMARK OFFICE. A COMPLETE MICROFILM COPY IS AVAILABLE AT THE ASSIGNMENT SEARCH ROOM ON THE REEL AND FRAME NUMBER REFERENCED BELOW.

PLEASE REVIEW ALL INFORMATION CONTAINED ON THIS NOTICE. THE INFORMATION CONTAINED ON THIS RECORDATION NOTICE REFLECTS THE DATA PRESENT IN THE PATENT AND TRADEMARK ASSIGNMENT SYSTEM. IF YOU SHOULD FIND ANY ERRORS OR HAVE QUESTIONS CONCERNING THIS NOTICE, YOU MAY CONTACT THE EMPLOYEE WHOSE NAME APPEARS ON THIS NOTICE AT 703-308-9723. PLEASE SEND REQUEST FOR CORRECTION TO: U.S. PATENT AND TRADEMARK OFFICE, ASSIGNMENT DIVISION, BOX ASSIGNMENTS, CG-4, 1213 JEFFERSON DAVIS HWY, SUITE 320, WASHINGTON, D.C. 20231.

RECORDATION DATE: 09/08/1998

REEL/FRAME: 9431/0438
NUMBER OF PAGES: 7

BRIEF: ASSIGNMENT OF ASSIGNOR'S INTEREST (SEE DOCUMENT FOR DETAILS).

ASSIGNOR:

CUTTITTA, FRANK

DOC DATE: 08/11/1998

ASSIGNOR:

MARTINEZ, ALFREDO

DOC DATE: 08/11/1998

ASSIGNOR:

MILLER, MAE JEAN

DOC DATE: 08/11/1998

ASSIGNOR:

UNSWORTH, EDWARD J.

DOC DATE: 08/11/1998

ASSIGNOR:

HOOK, WILLIAM

DOC DATE: 08/11/1998

ASSIGNOR:

WALSH, THOMAS

DOC DATE: 08/11/1998

ASSIGNOR:

GRAY, KAREN

DOC DATE: 08/11/1998

RECEIVED
JAN 12 1999
MORGAN & FINNEGAN LLP

ASSIGNOR:
MACRI, CHARLES

DOC DATE: 08/11/1998

ASSIGNEE:
NATIONAL INSTITUTES OF HEALTH, AS
THE REPRESENTED BY THE
SECRETARY, DEPARTMENT OF HEALTH
AND HUMAN SERVICES, THE
6011 EXECUTIVE BOULEVARD
OFFICE OF TECHNOLOGY TRANSFER,
SUITE 325
ROCKVILLE, MARYLAND 20852

SERIAL NUMBER: 09011922
PATENT NUMBER:

FILING DATE: 02/17/1998
ISSUE DATE:

TONYA LEE, EXAMINER
ASSIGNMENT DIVISION
OFFICE OF PUBLIC RECORDS

AUTHORIZATION

Should any additional fees be deemed to be properly assessable in this application, the Commissioner is hereby authorized to charge Deposit Account No. 13-4500, Order No. 2026-4202US4. **A duplicate copy of this sheet is attached.**

Respectfully submitted,

MORGAN & FINNEGAN, L.L.P.

Date: August 16, 2000

By: _____

Leslie A. Serunian

Leslie A. Serunian

Registration No. 35,353

Correspondence Address:

MORGAN & FINNEGAN, L.L.P.

345 Park Avenue

New York, New York 10154-0053

Telephone: (212) 758-4800

Facsimile: (212) 751-6849